Please amend the subject application as follows:

In the Claims

Please cancel claims 55-57 without prejudice to applicants rights to pursue the subject matter of these claims in this or a subsequent application.

Please amend claims 1, 3, 5, 14-16, 23-32, 50, 52-54, 58 and 61-64, and add new claims 73-91 under the provisions of 37 C.F.R. §1.121(c). The amended claims are presented below and the amendments to the claims are indicated in the marked-up set of claims attached hereto.

1. (Amended) A homogeneous crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14, and 26.91.

3. (Amended) A crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, which is free of the A polymorph.

5. (Amended) A composition comprising a crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine

designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, and a carrier, wherein the composition is free of the A polymorph.

14. (Twice Amended) A method of treating abnormal cell growth of a cell expressing the epidermal growth factor receptor (EGFR) in a mammal which comprises administering to said mammal a therapeutically effective amount of the polymorph of claim 3.

15. (Amended) The method of claim 14, wherein the abnormal cell growth is brain, squamous cell, bladder, gastric, pancreatic, hepatic, glioblastoma multiforme breast, head, neck, esophageal, prostate, colorectal, lung, renal, kidney, ovarian, gynecological or thyroid cancer.

16. (Amended) The method of claim 14, wherein the abnormal cell growth is non-small cell lung cancer (NSCLC), refractory ovarian cancer, or head and neck cancer.

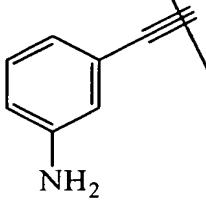
23. (Twice Amended) A method for the treatment of abnormal cell growth of a cell expressing the epidermal growth factor receptor (EGFR) in a mammal which comprises administering to said mammal a therapeutically effective amount of the polymorph of claim 3 in combination with an anti-tumor agent selected from the group consisting of a mitotic inhibitor, an alkylating agent, an anti-metabolite, an intercalating antibiotic, a growth factor inhibitor, a cell cycle inhibitor, an enzyme, a

topoisomerase inhibitor, a biological response modifier, an anti-hormone, and an anti-androgen.

24. (Amended) A process for preparing a crystalline polymorph of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride designated the B polymorph, which is free of the A polymorph, which comprises the step of recrystallizing N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in a solvent comprising alcohol.

25. (Amended) The process of claim 24, wherein the solvent further comprises water.

26. (Amended) The process of claim 24, wherein N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride is prepared by coupling a compound of formula 6



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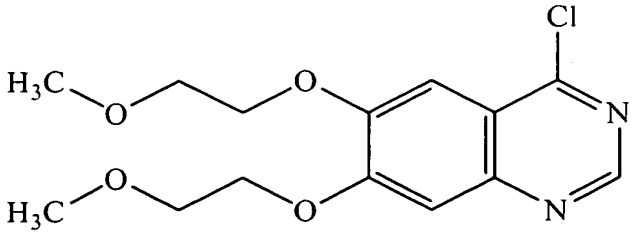
with a compound of formula 4



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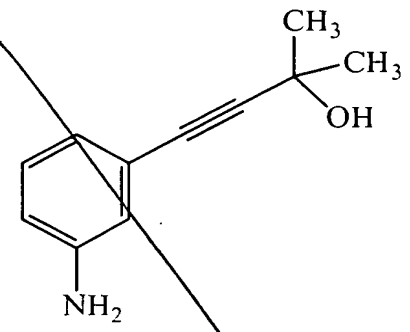
27. (Amended) The process of claim 26, wherein said compound of formula 6 is prepared by heating a compound of formula 5



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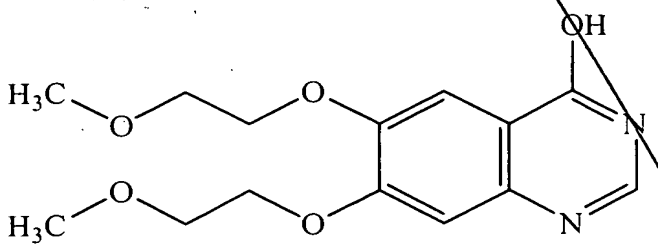
in a suspension of metal alkali and solvent.

28. (Amended) The process of claim 26, wherein said compound of formula 4 is prepared by chlorinating a compound of formula 3



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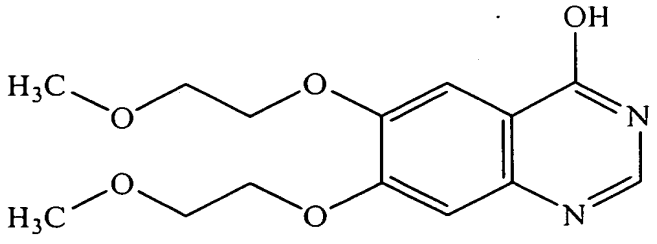
29. (Amended) A process for the production of the polymorph B of claim 1 comprising the steps of:

a) substitution chlorination of starting quinazolinamine compound of formula 3



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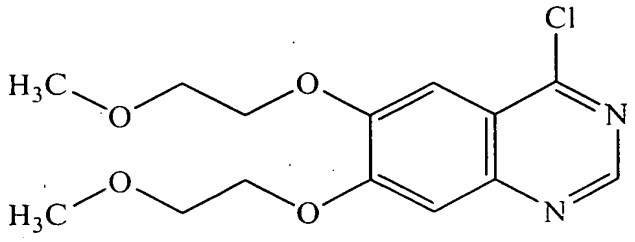
having an hydroxyl group, to provide a compound of formula 4



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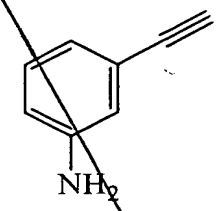
by reaction thereof in a solvent mixture of thionyl chloride, methylene chloride and dimethylformamide,

b) preparation of a compound of formula 6



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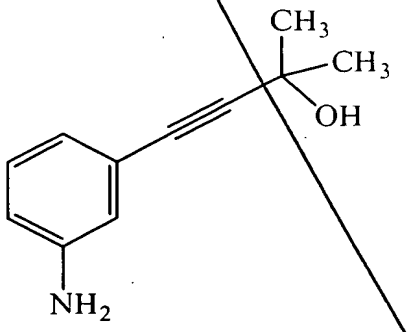
in situ from starting material of compound of formula 5



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by heating the compound of formula 5 in a suspension of metal alkali and solvent;

c) reaction of the compound of formula 6 in situ with the compound of formula 4 wherein the compound of formula 6 replaces the chlorine in the compound of formula 4 to give the N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride;

d) recrystallizing the N-(3-ethynylphenyl)-6,7-bis(2-

methoxyethoxy)-4-quinazolinamine hydrochloride, in alcohol, into the polymorph B form.

58. (Amended) The process of claim 29, wherein the substitution chlorination is quenched in the presence of aqueous sodium hydroxide.

59. (Amended) The process of claim 29, wherein the substitution chlorination is quenched in the presence of aqueous sodium bicarbonate.

60. (Amended) The process of claim 29, wherein the substitution chlorination is quenched in the presence of aqueous potassium hydroxide, aqueous potassium bicarbonate, aqueous potassium carbonate, aqueous sodium carbonate, or a mixture thereof.

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50. (Twice Amended) A method of inhibiting the development of basal or squamous cell carcinoma of the skin in areas exposed to the sun or in persons of high risk to said carcinoma, said method comprising administering to said persons a therapeutically effective amount of a pharmaceutical composition comprised of at least one of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine, and pharmaceutically acceptable salts thereof in anhydrous and hydrate forms, so as to thereby inhibit the development of basal or squamous cell carcinoma of the skin.

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52. (Amended) A process of making a composition which composition comprises a crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B

polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, which is free of the A polymorph, comprising admixing the crystalline polymorph with a carrier.

53. (Amended) The process of claim 52, wherein the N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in the polymorph B form is characterized by the X-ray powder diffraction pattern shown in Figure 3.

54. (Amended) The process of claim 52, wherein the carrier is a pharmaceutically acceptable carrier.

58. (Amended) A pharmaceutical composition which comprises a therapeutically effective amount of the polymorph of claim 3 and a pharmaceutically acceptable carrier, wherein the pharmaceutical composition is free of the A polymorph.

61. (Amended) A process for the production of a crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph by recrystallization comprising the steps of:

a) heating to reflux alcohol, water and the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine so as to form a solution;

b) cooling the solution to between about 65 and 70 °C;

c) clarifying the solution; and

d) precipitating polymorph B by further cooling the clarified solution.

62. (Amended) A composition consisting of a homogeneous crystalline polymorph of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in the form of polymorph B, which is characterized by the following peaks:

Polymorph B

Anode: Cu - Wavelength 1 1.54056 Wavelength 2: 1.54439 (Rel Intensity:0.500)
Range # 1 - Coupled 3.000 to. 40.040 StepSize: 0.040 StepTime 1.00
Smoothing Width: 0.300 Threshold: 1.0

d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)
14.11826	100.0	5.01567	2.5	3.86656	4.8	3.23688	0.9	2.74020	1.7
11.23947	3.2	4.87215	0.7	3.76849	2.3	3.16755	1.5	2.69265	1.7
9.25019	3.9	4.72882	1.5	3.71927	3.0	3.11673	4.3	2.58169	1.5
7.74623	1.5	4.57666	1.0	3.63632	6.8	3.07644	1.4	2.51043	0.8
7.08519	6.4	4.39330	14.4	3.53967	10.0	2.99596	2.1	2.47356	1.0
6.60941	9.6	4.28038	4.2	3.47448	3.7	2.95049	0.9	2.43974	0.6
5.98828	2.1	4.20645	14.4	3.43610	3.9	2.89151	1.6	2.41068	1.1
5.63253	2.9	4.06007	4.7	3.35732	2.8	2.83992	2.2	2.38755	1.4
5.22369	5.5	3.95667	4.5	3.31029	5.6	2.81037	2.4	2.35914	1.7

or,

Polymorph B

Anode: Cu - Wavelength 1 1.54056 Wavelength 2: 1.54439 (Rel Intensity:0.500)
Range# 1 - Coupled: 3.000 to 40.040 StepSize 0.040 StepTime: 1.00
Soothing Width:0.300 Threshold: 1.0

2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)
6.255	100.0	17.668	2.5	22.982	4.8	27.534	0.9	32.652	1.7
7.860	3.2	18.193	0.7	23.589	2.3	28.148	1.5	33.245	1.7
9.553	3.9	18.749	1.5	23.906	3.0	28.617	4.3	34.719	1.5
11.414	1.5	19.379	1.0	24.459	6.8	29.000	1.4	35.737	0.8
12.483	6.4	20.196	14.4	25.138	10.0	29.797	2.1	36.288	1.0
13.385	9.6	20.734	4.2	25.617	3.7	30.267	0.9	36.809	0.6
14.781	2.1	21.103	14.4	25.908	3.9	30.900	1.6	37.269	1.1
15.720	2.9	21.873	4.7	26.527	2.8	31.475	2.2	37.643	1.4
16.959	5.5	22.452	4.5	26.911	5.6	31.815	2.4	38.114	1.7

and at least one carrier.

63. (Amended) A method of treating a subject with a tumor by inducing differentiation of tumor cells expressing an epidermal growth factor receptor (EGFR) in the tumor comprising contacting the cells with an effective amount of the compound of claim 3, or a composition of claim 5 so as to thereby treat the subject.

64. (Amended) A method for the treatment of NSCLC (non small cell lung cancer), pediatric malignancies, cervical and other tumors caused or promoted by human papilloma virus (HPV), endometrial cancer, glioma, melanoma, Barrett's esophagus (pre-malignant syndrome), adrenal cancers, neoplastic cutaneous diseases or atherosclerosis in a mammal comprising administering to said mammal a therapeutically effective amount of a pharmaceutical composition comprised of at least one of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine, and pharmaceutically acceptable salts thereof in anhydrous and hydrate forms.

Please add new claims 73-91 as follows:

73. (New) The method of claim 64, wherein the pharmaceutical composition comprises a crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.86, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, and a pharmaceutically acceptable carrier, wherein the composition is free of the A polymorph.

34 74. (New) A method for the treatment of NSCLC (non small cell lung cancer), pediatric malignancies, cervical and other tumors caused or promoted by human papilloma virus (HPV), endometrial cancer, glioma, melanoma, Barrett's esophagus (pre-malignant syndrome), adrenal and skin cancers, autoimmune, neoplastic cutaneous diseases or atherosclerosis in a mammal comprising administering to said mammal a therapeutically effective amount of a pharmaceutical composition comprised of at least one of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine, and pharmaceutically acceptable salts thereof in anhydrous and hydrate forms,

E12

wherein the treatment further comprises,

Sub E1

a) treatment with either or both anti-EGFR and anti-EGF antibodies,

b) administration to said mammal of a member of the group consisting of inhibitors of MMP (matrix-metallo-proteinase), VEGFR (vascular endothelial growth factor receptor), farnesyl transferase, $CTLA_4$ (cytotoxic T-lymphocyte antigen 4) and erbB2, MAb to VEGFr, rhuMAb-VEGF, erbB2 MAb and avb3 Mab, or

c) radiation treatment.

35 75. (New) The method of claim 13, wherein the abnormal cell growth is pancreatic cancer.

36 76. (New) The method of claim 13, wherein the abnormal cell growth is colorectal cancer.

37 77. (New) The method of claim 13, wherein the abnormal cell growth is prostate cancer.

38 78. (New) The method of claim 13, wherein the abnormal cell growth is breast cancer.

39 79. (New) The method of claim 13, wherein the abnormal cell growth is esophageal cancer.

40 80. (New) The method of claim 13, wherein the abnormal cell growth is ovarian cancer.

Sub E1 41 81. (New) The method of claim 13, wherein the abnormal cell growth is glioblastoma multiforme.

C2 42 82. (New) The method of claim 13, wherein the abnormal cell growth is hepatic cancer.

43 83. (New) The method of claim 13, wherein the abnormal cell growth is renal cancer.

44 84. (New) The method of claim 13, wherein the abnormal cell growth is gastric cancer.

45 85. (New) The method of claim 13, wherein the abnormal cell growth is bladder cancer.

46 86. (New) The method of claim 14, wherein the abnormal cell growth is non-small cell lung cancer (NSCLC).

47 87. (New) The method of claim 14, wherein the abnormal cell growth is head and neck cancer.

48 88. (New) The method of claim 29 for the treatment of non-small cell lung cancer (NSCLC).

C

89. (New) The method of claim 64 for the treatment of endometrial cancer.

90. (New) The method of claim 64 for the treatment of glioma.

91. (New) The method of claim 64 for the treatment of melanoma.